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ONE STEP SYNTHESIS OF AZIRIDINES BY THE MICHAEL TYPE ADDITION OF FREE SULFIMIDES

PREPARATION AND ABSOLUTE CONFIGURATION OF OPTICALLY ACTIVE ACYLAZIRIDINES

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Abstract—The Michael type additions of diphenyl N-unsubstituted sulfimide (free sulfimide) to various electrophilic olefins were carried out. The reaction with *cis*- and *trans*-dibenzoylethylene, dimethylfumarate, dimethylmaleate, benzalacetophenone and benzalacetone gave mainly the corresponding *trans*-2-acylaziridines and *trans*-enaminoketones. However, phenyl vinyl sulfone or acrylonitrile afforded not the corresponding aziridine but diphenyl-N-2-cyano or N-2-phenylsulfonylethylsulfimide, a simple Michael adduct. When optically active (+)-(*R*)-*o*-methoxyphenylphenyl free sulfimide was treated with such an α,β-unsaturated carbonyl compound as benzalacetophenone, an optically active 2-acylaziridine, i.e., (−)-*trans*-2-benzoyl-3-phenylaziridine was obtained in *ca* 30% optical purity and its absolute configuration was assigned as (2*R*,3*S*) upon chemical transformation to the configurationally known 2-phenyl-2-benzoylamino-1-ethanol or by comparing its CD spectrum with that of (1*R*,2*R*)-1-phenyl-2-benzoyl-cyclopropane. Meanwhile, (−)-(*S*)-*o*-methoxyphenylphenyl free sulfimide was found to react with benzalacetophenone to afford (+)-trans-2-benzoyl-3-phenylaziridine of 25% optical purity. Effects of solvent and temperature on both the distribution of the products ratio and the optical yield were examined.

THE chemistry of sulfimides has been developed[1] since the discovery of convenient procedures to prepare free sulfimides.[2] Generally, free sulfimides are found to be relatively strong bases and good nucleophiles; e.g., pKa of diphenyl free sulfimide is 8.5.[3] Actually diphenyl free sulfimide is readily acylated or alkylated with various acylating or alkylating reagents to afford the corresponding N-acylated or N-alkylated sulfimide.[2a,b]

Diphenyl free sulfimide was found to undergo the Michael type addition to such electrophilic olefins as *trans*-dibenzoylethylene and benzalacetophenone to afford the corresponding aziridine derivatives and enaminoketones in moderate yields.[4] Meanwhile, we found a convenient method to prepare the optically active *o*-methoxyphenyl- or *o*-methylphenylphenyl-N-*p*-tosylsulfimide by treating the addition complex between the corresponding sulfide, t-butyl hypochlorite and *l*-menthol with tosylamide anion.[5] A combination of these two processes, namely the preparation of free and optically active sulfimide and the Michael type addition to electrophilic olefins may promise a convenient one step synthesis of optically active aziridine derivatives. In the preliminary communication,[6] we briefly reported the preparation of optically active aziridine derivatives by the Michael type addition of optically active diaryl free sulfimide to electrophilic olefins.

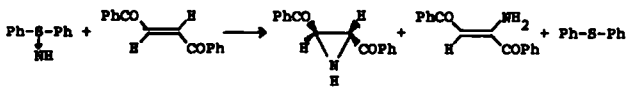
This paper gives a full account of this useful reaction to synthesize both non-optically active and optically active aziridines in one step, the absolute configuration of optically active *trans*-2-benzoyl-3-phenylaziridine and the stereochemistry of the reaction, together with the plausible mechanism of the reaction.

RESULTS AND DISCUSSION

The reaction of diphenyl free sulfimide with electrophilic olefins

Diphenyl free sulfimide (**1**) was prepared according to our procedure, namely by treatment of diphenyl-N-*p*-tosylsulfimide with conc sulfuric acid.[2a] Generally, the Michael type addition of **1** to electrophilic olefins was carried out using a slight excess of **1** with e.g., *trans*-dibenzoylethylene (**2**) at room temperature for one hour in benzene solution. After the general work up, *trans*-2,3-dibenzoylaziridine (**3**) and 1,2-dibenzoyl-1-aminoethylene (**4**) were obtained in *ca* 50% yields respectively together with diphenyl sulfide (**5**) in a quantitative yield (Scheme 1). These products were identified by IR, NMR, mass spectra and elemental analyses. Dimethylfumarate, dimethylmaleate and benzalacetophenone are less reactive than dibenzoylethylene and it was necessary to heat the mixture for a prolonged time. Acrylonitrile and phenyl vinyl sulfone were treated similarly with **1** in benzene solution and simple Michael addition products were obtained. These results obtained are listed in Table 1.

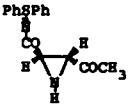
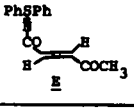
The structure of aziridine **3** was confirmed by



1 **2** **3** **4** **5**

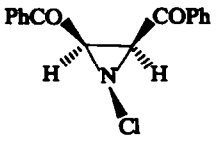
Scheme 1.

Table 1. Reaction of electrophilic olefins with diphenyl free sulfimide in benzene

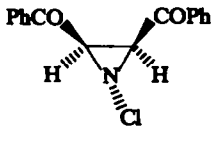
Olefin X^1-CH=CH-X^2	Ratio Sulfimide: Olefin	Conditions (time/temp)	PhSPh	Products and Yields (%)		Recovered Olefin	Others
	1.2	1h/r.t.	100	50[a]	50	0	-
	1.2	1h/r.t.	100	43[a]	55	0	-
	0.5	1h/r.t.	100	15[a]	34	53[b]	-
	1.2	24h/reflux	91[c]	46[a]	23[d]	4	D(9%), E(6%)
	1.2	24h/reflux	64[c]	40[a]	26[d]	12[e]	- 
	2.0	24h/reflux	140[c]	73	-	12	-
	1.2	36h/50°C[f] MeOH	89	67	-	20	- D
H_2C=CH-CN	0.83[g]	24h/reflux	Ph_2S→NCH$_2$CH$_2$CN (69%)[h]				- 
	0.89	1h/r.t.	Ph_2S→NCH$_2$CH$_2$SO$_2$C$_6$H$_5$ (100%)[h]				-

a) Configuration assigned as trans by comparison with the corresponding N-chloro derivative. b) 31% cis, 22% trans. c) Contains sulfide from thermal decomposition of free sulfimide. d) Configuration assigned as trans by comparison of ir, nmr, and uv spectra with those of an authentic sample. e) Only trans-form was recovered. f) Small amount of methanol was used. g) No solvent was used. h) Yields are based on free sulfimide.

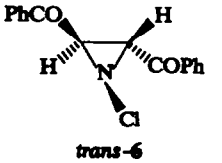
converting it with t-butyl hypochlorite to the corresponding N-chloroaziridine (**6**).[7] The NMR signals of the methine protons of **3** are broad, indicating that the pyramidal inversion around the N atom is relatively slow on the NMR time scale.[8,9] Whereas, the chloro derivatives (**6**) which are considered to undergo no pyramidal inversion at room temperature, should give sharp NMR signals. If **3** has the *cis*-configuration shown below, then the methine signal of **6** should be a singlet, while that of *trans*-configuration should give an AB quartet. Actually, **6** gave an AB quartet signal centered at $\delta = 4.31$ and 4.47 ppm corresponding to the 2,3-methine protons indicating clearly that **3** has the *trans*-configuration.



cis-**6**



cis-**6**



trans-**6**

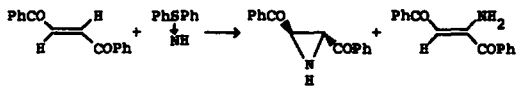
Although the configuration of **4** has not been fully established, the IR spectra of **4** taken in carbon tetrachloride at various concentrations indicate strong H-bonding between the amino hydrogen and the carbonyl oxygen suggesting that **4** has a *trans*-configuration. The reactions of both *cis*- and *trans*-**2** gave only the *trans* isomers of **3** and **4** which are thermodynamically more stable than the *cis*-isomer. Similarly, both dimethylfumarate and dimethylmaleate afforded only the corresponding *trans*-aziridine and the enamine but not the *cis* isomer. Thus, this addition-elimination reaction is non-stereospecific.

When an excess *cis*-dibenzoylethylene was treated with **1**, the recovered olefin was found to be composed of both *cis* and *trans* isomers. Furthermore, when dimethylmaleate was used as the starting material, the recovered olefin was transformed completely to the fumarate in refluxing benzene. This *cis-trans* isomerization did not take place under the same reaction conditions without the free sulfimide, indicating that the initial step of this Michael type addition is a reversible formation of the intermediate carbanion. In constrast to dibenzoylethylene, dimethylfumarate, dimethylmaleate and benzalacetophenone, the reactions of acrylonitrile and phenyl vinyl sulfone with **1** did not give the corresponding aziridine derivatives but afforded the N-2-cyano- and N-2-phenylsulfonylethylsulfimide in good yields.

The effects of solvent and temperature on the ratio of the products **3** and **4**, i.e., $r = 3/4$, were examined by treating **1** and **2** of roughly 0.1 mol concentration in various solvents. The product ratios thus obtained are summarized in Table 2.

Inspection of the data in Table 2 reveals clearly that the aziridine formation is favored in aprotic solvents, while in methanol the enaminoketone **4** was the predominant product. The aziridine formation increased when the temperature was raised in

Table 2. Effects of solvent and temperature



Solvent	Temp(°C)	γ(aziridine/enaminoketone)
C_6H_6	18.0	0.40
	28.0	1.0
	35.0	1.63
CH_2Cl_2	28.0	0.27
CH_3OH	28.0	0.063
$(CH_3)_2SO$	28.0	0.39
C_6H_5N	28.0	0.47

benzene. On the basis of these observations, we propose the following mechanism for the formation of aziridine (3) and enaminoketone (4) (Scheme 2).

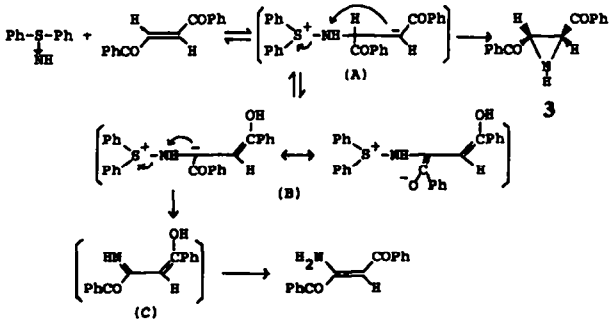
Addition of the free sulfimide to 1,2-dibenzoylethylene gives the carbanion **A**, which is stabilized by a CO group, will undergo prototropic conversion to form the carbanion **B**. Upon losing diphenyl sulfide from the intermediate **B** the final enaminoketone was formed via the intermediate **C**. The aziridine is undoubtedly formed by simple 1,3-internal elimination of **A**. This mechanistic scheme explains why the product varies by the change of the electrophilic olefin. In the reaction with benzalacetophenone, the initial Michael type addition intermediate which corresponds to **A** should be formed readily because of the stabilization by the CO group, however, the α-proton is not acidic enough to undergo prototropic migration and hence the second intermediate corresponding to **B** may not be formed. Thus, there is no formation of enaminoketone and the only product obtained was the aziridine. In the reaction of acrylonitrile or phenyl vinyl sulfone, the resulting addition intermediate carbanion is electronically less stabilized than those of the previous two olefins. In a polar protic solvent such as methanol the intermediate (**A**) may not survive long but **B** should be stabilized substantially by H-bonding. Thus the reaction is considered to result mainly in the formation of enaminoketone. Whereas in a nonpolar aprotic solvent such as benzene there is no stabilization due to protonation or H-bonding to favor the enaminoketone formation. Therefore, the carbanion once formed may attack the imino N atom, affording the aziridine. Similar mechanisms are known to operate in both epoxidation[10] and cyclopropane formation.[11] Accordingly, in order to increase the yield of the aziridine derivative, the reaction should be conducted in a nonpolar aprotic solvent at a relatively higher temperature and with a moderate concentration of the substrate.

Synthesis of optically active aziridines

Preparation of optically active free sulfimide. Optically active diaryl free sulfimides were prepared from the corresponding N-*p*-tosyl derivatives which were obtained by either one of the following two methods. Method A (Asymmetric induction and recrystallization):[5] Previously we reported a convenient procedure to prepare optically active *o*-methoxyphenylphenyl-N-*p*-tosylsulfimide by treating a mixture of the corresponding sulfide, t-butyl hypochlorite and *l*-menthol with tosylamide anion in the presence of pyridine. The optically pure sulfimide was prepared readily by repeated recrystallizations of the crude crystals. Method B (Inoculation method): In this method the optically pure (*R*)- or (*S*)-*o*-methoxyphenylphenyl-N-*p*-tosylsulfimide prepared by the method A was used as seeds for crystallization in order to obtain the optically pure enantiomer from the racemate. A small amount of the (*R*)- or (*S*)-*o*-methoxyphenylphenyl-N-*p*-tosylsulfimide was added to the racemic N-*p*-tosylsulfimide in hot acetone solution. This solution was kept standing for 1–2 days at room temperature until the crystallization was complete. By this method (*R*)- or (*S*)-*o*-methoxyphenylphenyl-N-*p*-tosylsulfimide was separated nearly in pure form. The optical purity of the sulfimide thus obtained ranged from 95–100% depending upon the temperature and the amount of the solvent. Therefore, if a large amount of the optically pure sulfimide, e.g., 100 g, is necessary, the method B is better than the method A since the racemic N-*p*-tosylsulfimide can be prepared very readily from the sulfide and chloramine-T.[12]

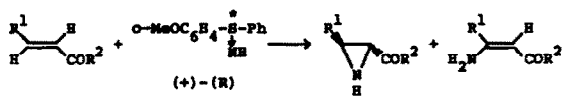
Preparation of optically active aziridine by asymmetric induction. One step synthesis of optically active aziridines by the Michael type addition was carried out initially by treating (+)-(*R*)-*o*-methoxyphenylphenyl free sulfimide with several electrophilic olefins. Then the products were separated carefully by column chromatography avoiding fractionation of the products. The products thus obtained were identified by comparison of the IR and NMR spectra with those of the racemic authentic samples and the results are summarized in Table 3.

Inspection of the results clearly indicate that the



Scheme 2.

Table 3. Syntheais of optically active aziridines



Olefins R^1	R^2	Optical purity of the sulfimide (%)	Conditions	Products and Yields (%) (I)[a]	(II)	$[\alpha]_D^{25}$	Optical purity[b] (%)
PhCO	Ph	84.8	C_6H_6, r.t., 1h	30[c]	68	-32.9°	-
PhCO	Ph	96.8	CH_3OH, 30°C, 1h	8[c]	90	-29.0°	-
PhCO	Ph	96.8	DMSO, 28°C, 1h	61[c]	37	-20.0°	-
Ph	Ph	84.8	CH_2Cl_2, 50°C, 48h	66[d]	0	-88.0°	28.7
Ph	Ph	96.8	CH_3OH, 50°C, 12h	46[d]	0	-87.1°	28.4
Ph	Ph	96.8	CH_3OH, r.t., 6days	53[d]	0	-93.3°	30.4
Ph	Ph	96.8	C_6H_6, 50°C, 48h	96[d]	0	-99.0°	32.6
Ph	Me	84.8	C_6H_6, 50°C, 24h	23[d]	0	-60.0°	-
cis-PhCO	Ph	96.8	C_6H_6, r.t., 1h	33[c]	21	-35.6°	-
PhCO	Ph	98.5[e]	C_6H_6, 20°C, 1h	59[c]	-	+23.2°	-
Ph	Ph	86.9[e]	CH_2Cl_2, 50°C, 48h	22[c]	-	+77.5°	25.3
Ph	$=(COOMe)_2$	78.8	CH_2Cl_2, 50°C, 48h	42[c]	-	-22.0°	-

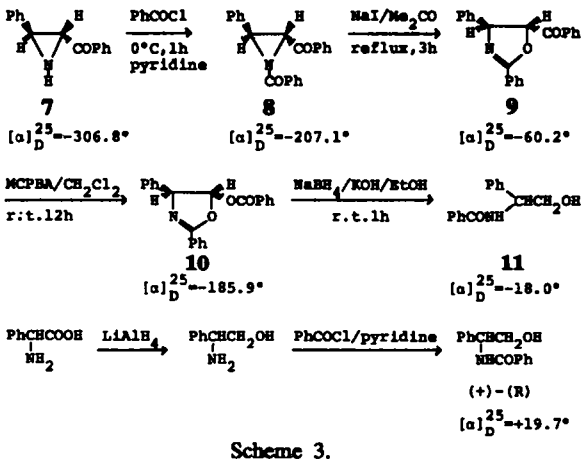
a) All aziridines were found to have trans configuration which was identified by methine-methine coupling constant of the nmr.
b) All the specific rotations were measured in chloroform solution.
c) Other product was o-methoxyphenyl phenyl sulfide (~100%).
d) Other product was o-methoxyphenyl phenyl sulfide and the starting olefin was recovered. e) (-)-(S)-sulfimide was used.

Michael type addition of the optically active free sulfimide to electrophilic olefins took place exactly in the same manner as that of diphenyl free sulfimide, but affording the optically active aziridines. In the reaction of *trans*-dibenzoylethylene, (−)-*trans*-2,3-dibenzoylaziridine and *trans*-1-amino-1,2-dibenzoyethylene were obtained in substantial yields. The optical rotation of this aziridine decreased upon repeated recrystallizations and hence the optical purity of this product could not be estimated. Whereas, in the reaction of benzalacetophenone, the products obtained were the corresponding aziridine and the sulfide without a trace of the enaminoketone, while the optical rotation of the resulting aziridine, 2-benzoyl-3-phenylaziridine, increased by several repeated recrystallizations from methanol, finally attaining $[\alpha]_D^{25} = -306.8°$. If this optical rotation is considered as the maximum value, the optical purity of the aziridine formed in the Michael type addition is estimated around 30% though the optical purity of the product fluctuates slightly as the reaction condition changed. In order to examine the effect of solvent on the aziridine formation, a few reactions were carried out in different solvents. Inspection of the results shown in Table 3 reveals that the product ratio of aziridine (1) to enaminoketone (2) in the reaction of *trans*-1,2-dibenzoylethylene, is very sensitive to the solvent, in keeping with the similar results with 1,2-dibenzoylethylene shown in Table 2. Meanwhile, the extent of asymmetric induction varied rather little by the change of the solvent and temperature employed. Meanwhile, the analogous treatment of benzalacetophenone with (−)-(*S*)-*o*-methoxyphenylphenyl free sulfimide afforded the corresponding (+)-aziridine in 25% optical purity as shown in Table 3.

Absolute configuration of (−)-trans-2-*benzoyl*-3-*phenylaziridine*

The absolute configurations of only a few optically active aziridine derivatives have been reported in the literature,[13] but unrelated to our compounds. Therefore, in order to determine the absolute configuration of (−)-*trans*-2-benzoyl-3-phenylaziridine (7), degradation of the aziridine (7) to the N-benzoyl-1-phenylethanolamine (11) via several steps were carried out as shown in Scheme 3. Namely, the aziridine (7) was first converted to the N-benzoyl derivative (8)[14] which was then treated with sodium iodide in acetone to afford the isoxazole derivative (9).[15] Then, the isoxazole (9) was treated with *m*-chloroperbenzoic acid (MCPBA) to obtain the Bayer-Villiger rearranged product **10** which was reduced finally to the ethanolamine (11).[16] During these transformations, the optical activity on C atom 2 is lost, while the configuration on C atom 3 should not change. Therefore, the stereochemistry on both C atoms 2 and 3 can be determined by these methods. After the aziridine (7) was converted to the ethanolamine (11), the sign and magnitude of optical rotation of the ethanolamine (11) were compared with those of the other ethanolamine (11) obtained from (−)-phenylglycine of which the configuration is known to be (*R*).[17] Consequently, the sign of the optical rotation of 11 obtained from 7 was found to be opposite to that derived from the optically active phenylglycine, though the values of optical activities are slightly different. Since the latter is known to have the (*R*)-configuration, the absolute configuration of the carbon atom 3 in the aziridine (7) can be assigned as (*S*). Thus, the configuration of C atom 2 of 7 is assigned automatically as (*R*). Thus, the (−)-*trans*-aziridine (7) formed in the Michael type addition is determined to have configuration (2*R*,3*S*).

CD spectrum of (−)- *and* (+)-trans-2-*benzoyl*-3-*phenylaziridine*. As an alternative method to determine the configuration of the aziridine, the CD spectrum of 7 was taken and compared with that of (−)-*trans*-1-benzoyl-2-phenylcyclopropane (12) which was prepared by Johnson and has a known configuration of (1*R*,2*R*).[18] Recently, Cram *et al*



Scheme 3.

determined the absolute configuration of (+)-(*S*)-N-phenyl-*p*-toluenesulfinamide by comparison of its ORD spectrum with that of carbon analog, (+)-(*R*)-benzyl *p*-tolyl sulfoxide.[19] The CD curve of **7** obtained is similar to that of cyclopropane (**12**). Both have similar Cotton effects ($[\theta]_{232}=+23{,}000$, $[\theta]_{263}=-29{,}700$, $[\theta]_{315}=-13{,}900$ for **7** and $[\theta]_{260}=-25{,}600$, $[\theta]_{312}=-15{,}700$ for **12**). The CD spectra of both (−)- and (+)-**7** are shown in Fig. 1. The similar patterns of CD curves of both **7** and **12** served as evidence to support that the absolute configuration of **7** and **12** are identical, in keeping with the result of the chemical assignment of the absolute configuration of **7**. Although the (+)-aziridine is not optically pure, its CD spectrum shown together with that of (−)-**7** in Fig. 1 clearly reveals that the Cotton effect of this compound opposite to that of the (−)-derivative.

In the literature, two methods to prepare N-unsubstituted 2-acylaziridine have been reported, one is the aminolysis of α,β-dibromoketone (or α-bromo-α,β-unsaturated ketone),[20] and the other is the two step synthesis involving the Michael addition of methoxyamine to α,β-unsaturated ketone followed by treatment of the adduct with base.[21] However, these reactions are rather complicated and produce many by-products. A few methods to prepare optically active N-unsubstituted aziridine are also known in the literature,[22] but involve many steps. Our present method is probably the simplest and the most convenient one step synthesis of optically active aziridines. The limitation of our procedure, however, is that this can be applied only to such electrophilic olefins as α,β-unsaturated carbonyl derivatives.

EXPERIMENTAL

All mps are uncorrected. The IR spectra were recorded on a Hitachi 215 Spectrometer, while the NMR spectra of the compounds in deuterated chloroform were recorded by a Hitachi R-24A High Resolution NMR Spectrometer using TMS as the internal standard. The optical rotations were determined with a Union OR-50D automatic Polarimeter and CD spectra were taken with JASCO J-20 Automatic Recording Spectropolarimeter.

Diphenyl free sulfimide was prepared according to our

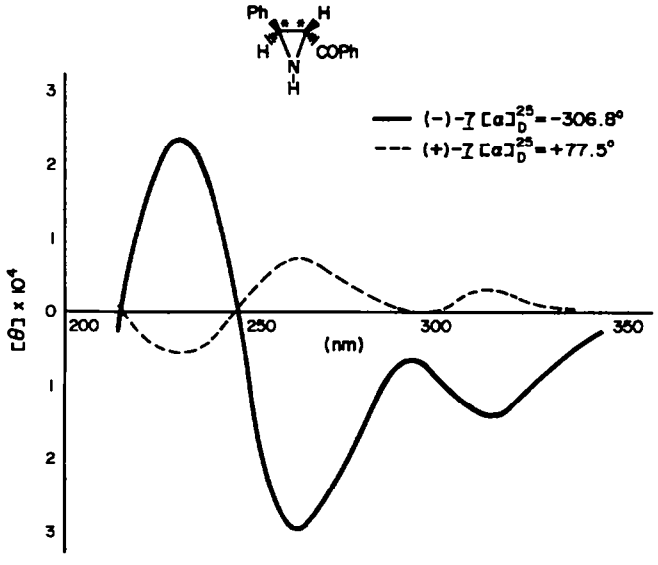


Fig. 1. CD-Spectrum of 2-benzoyl-3-phenyl aziridine

method, starting from diphenyl-N-*p*-tosylsulfimide with conc H_2SO_4.[2a] The commercially available olefins were used without purification. All solvents used were purified before use.

trans-2,3-*Dibenzoylaziridine.* *trans*-Dibenzoylethylene (200 mg) and diphenyl free sulfimide (223 mg) were dissolved in 5 ml of benzene at 30°. The soln was stirred for 1 hr at 30°. After the reaction, benzene was removed *in vacuo* and the residue was chromatographed through a column packed with silica gel using $CHCl_3$ as an eluent. *trans*-2,3-Dibenzoylaziridine was obtained in 50% yield together with *trans*-1-amino-1,2-dibenzoylethylene (50%) and diphenyl sulfide (100%). The aziridine was identified by IR, NMR, mass and elemental analyses, mp. 105–6° (recrystallization from MeOH). (Found; C, 76.08, H, 5.50, N, 5.52 $C_{16}H_{13}NO_2$(251.3) Calcd; C, 76.48, H, 5.21, N, 5.57%). IR (KBr, cm^{-1}), 3240, 1670. NMR (δppm), 2.70 (s, broad, 1H, NH), 3.73 (S, broad, 2H, —CH—CH—), 7.90–8.15 (m, 4H), 7.30–7.70 (m, 6H). Mass, *m/e* (rel. intensity), 251 (1.9), 236 (0.37), 146 (100), 128(2.1), 119(3.5), 118(9.0), 117(6.3), 105(35.5).

The enaminoketone was identified by comparing its IR, NMR spectrum with those of the authentic material, mp. 136–7° (lit. 137.5°C).[7] The reaction with *cis*-dibenzoylethylene was carried out similarly and the products were the same as those of the *trans*-isomer.

trans-*Dibenzoyl*-N-*chloroaziridine.* Dibenzoylaziridine (137 mg) was dissolved in 1 ml of $CHCl_3$. To this soln was added t-butyl hypochlorite (71 mg) at 0°.[7] The soln was stirred for 1 hr at 0°, then $CHCl_3$ was removed *in vacuo* and the corresponding N-chloroaziridine was obtained quantitatively. The crude crystals were recrystallized from chloroform-benzene, mp. 120–1°. (Found; C, 67.29, H, 4.09, N, 4.79. $C_{16}H_{12}NO_2Cl$(285.8) Calcd; C, 67.26, H, 4.23, N, 4.90%). IR (KBr, cm^{-1}), 1680. NMR (δppm), 4.31, 3.37(q, 2H, —CH—CH—, J_{AB} = 5 Hz), 7.70–8.26(m, 4H), 7.40–7.70(m, 6H).

Intramolecular hydrogen bonding of 1-*amino*-1,2-*dibenzoylethylene.* IR spectra of the 1-amino-1,2-dibenzoylethylene were taken in CCl_4 at various concentrations (26.9, 10.1, 3.78, 1.42, 0.53 mM). For example, ν_{NH} 3470 (sharp, $\varepsilon = 180$, $\Delta\nu_{1/2} = 40$) and 3275 (broad, $\varepsilon = \Delta\nu_{1/2} = 80$), and $\nu_{C=O}$ 1670 ($\varepsilon = 180$), 1630 ($\varepsilon = 480$) at 3.78 mM. These IR absorption bands and their intensities were not affected by changing the concentration, indicating that the structure of this olefin has *trans*-configuration.

trans-2-*Benzoyl*-3-*phenylaziridine.* Diphenyl free sulfimide (210 mg) and benzalacetophenone (100 mg) were dissolved in 1 ml of benzene and the solution was refluxed for 16 hr. The work up process was analogous to that with dibenzoylethylene. In this case enaminoketone formation was not observed at all. The crude crystals thus obtained were recrystallized from MeOH, mp. 100–100.5°. IR (KBr, cm $^{-1}$), 3230, 1665. NMR (δppm), 2.57 (s, broad, 1H, NH), 3.19 (d, 1H, —CH—, J = 2.5 Hz), 3.53 (d, 1H, —CH—, J = 2.5 hz), 7.40–8.20 (m, 10H, Ph). The coupling constants of the methine protons indicate that the aziridine obtained has the *trans*-form.[14] Meanwhile, when the concentration was high and the temp was low, the yield of aziridine obtained was the best.

trans-2,3-*Dimethoxycarbonylaziridine.* Dimethylfumarate (200 mg) and diphenyl free sulfimide (366 mg) were dissolved in 3 ml of benzene and the soln was refluxed for 24 hr. The work up process was the same as that mentioned above. The corresponding *trans*-aziridine was obtained as an oily material in 46% yield together with *trans*-1-amino-1,2-dimethoxycarbonylethylene (23%) which was identified by comparing its IR, NMR, and UV spectra. *trans*-2,3-Dimethoxycarbonylaziridine, Found; C, 45.26, H, 5.45, N, 8.81. $C_6H_9NO_4$(159.1) Calcd; C, 45.28, H, 5.70, N, 8.80%). IR (film, cm^{-1}), 3270, 1735. NMR (δppm), 1.90 (s, broad, 1H, NH), 2.90 (s, 2H, —CH—CH—), 3.80 (s, 6H, CH_3).

Besides these two products, two other products, **D** and **E**, were isolated in 9 and 6% yields through chromatography, respectively. The IR and NMR spectra suggest that the structures of these products are **D** and **E**.

trans-2-Diphenylsulfimidoylcarbonyl-3-methoxycarbonylaziridine(D) (oil); IR (film, cm^{-1}), 3250, 1735, 1600. NMR (δppm), 2.03 (s, 1H, NH), 2.84 (d, 1H, —CH—, J = 2.5 Hz), 3.15 (d, 1H, —CH—, J = 2.5 Hz), 3.74 (s, 3H, CH_3), 7.45–7.90 (m, 10H, Ph).

Diphenyl-N-(*trans*-3-methoxycarbonylacryloyl)sulfimide (E) (oil); IR (film, cm^{-1}), 1725, 1595, 1575, NMR (δppm), 3.80 (s, 3H, CH_3), 6.68, 6.93, 7.20, 7.45 (AB, 2H, —CH═CH—, J_{AB} = 15 Hz), 7.45–8.0 (m, 10H, Ph).

trans-2,3-*Dimethoxycarbonyl*-N-*chloroaziridine.* This was prepared similarly as dibenzoylaziridine quantitatively (oil). IR (film, cm^{-1}) 1740. NMR (δppm), 3.44 (AB, 2H, —CH—CH—, $\Delta(\delta_{CH_A} - \delta_{CH_B}) = 0$, $J_{AB} = 4$ Hz), 3.78 (s, 3H, CH_3), 3.85 (s, 3H, CH_3).

Addition of diphenyl free sulfimide to acrylonitrile. Diphenyl free sulfimide (1.0 g) was dissolved in 290 mg of acrylonitrile and the soln was refluxed for 24 hr. Then the reaction mixture was cooled to room temp and diluted with 20 ml of 3% H_2SO_4 aq . The oil separated was removed by adding charcoal. The filtrate was made alkaline with NaOH aq. The heavy oil separated was extracted with $CHCl_3$. The $CHCl_3$ soln was dried over Na_2SO_4 and the solvent was removed *in vacuo*. The residue was obtained as an oil and identified as diphenyl-N-(2-cyanoethyl)sulfimide, yield was 0.8 g (69%). IR (film, cm^{-1}), 2250, 1100. NMR (δppm), 2.49 (t, 2H, NCH_2), 3.21 (t, 2H, —CH_2CN), 7.54 (s, 10H, Ph).

Addition of diphenyl free sulfimide to phenyl vinyl sulfone. Diphenyl free sulfimide (1.0 g) and phenyl vinyl sulfone (0.84 g) were dissolved in 30 ml of benzene at room temp. After 1 hr, the solvent was removed *in vacuo* and the same treatment as above afforded diphenyl-N-(2-phenylsulfonylethyl)sulfimide as an oil; yield, 1.70 g was quantitative. IR (film, cm^{-1}), 1305, 1140, 1081. NMR (δ ppm), 3.30, (s, broad, 4H, 2-CH_2), 7.40 (s, 10H, SPh), 7.40–7.90 (m, 5H, SO_2Ph).

Hydrolysis of diphenyl-N-(2-*phenylsulfonylethyl*)*sulfimide.* Diphenyl-N-(2-phenylsulfonylethyl)sulfimide (205 mg) was dissolved in 1 ml of conc HCl at room temp. After 10 min, the soln was diluted with 5 ml cold water and extracted with benzene. The benzene layer was washed with water, dried over Na_2SO_4. After removal of the solvent, diphenyl sulfoxide was obtained (108 mg, 96%). The aqueous layer was made alkaline and then extracted with $CHCl_3$. The usual work up gave 2-aminoethyl phenyl sulfone (76 mg, 75%) as an oil. IR (film, cm^{-1}), 3580, 3370 (broad). NMR (δppm), 1.87 (s, broad, 2H, NH_2), 2.9–3.5 (m, 4H, —CH_2CH_2—), 7.6–8.2 (m, 5H, Ph). The 2-aminoethyl phenyl sulfone was further converted to the hydrochloride salt, mp. 147–8°.

Resolution of optically active o-*methoxyphenylphenyl*-N-p-*tosyl-sulfimide by inoculation method.* Racemic *o*-methoxyphenylphenyl-N-p-tosylsulfimide (40 g) was dissolved into 850 ml of acetone by heating. When the soln was gradually cooled to about 30°, a small amount of optically pure (+)-isomer of the sulfimide finely pulverised was added as a kernel to the above soln. After keeping the soln at room temp, the crystals formed were collected and 0.6 gr of the (+)-isomer of the sulfimide was obtained, $[\alpha]_D^{25} = +95.1°$ (optical Purity, 97.0%). To this filtrate, 1.2 gr of the racemic sulfimide was added and the soln was heated until all the crystals were dissolved. The soln was cooled down to room temp and to this was added a small amount of the (−)-isomer of the sulfimide. the soln was kept standing overnight at room temp. The ppt was filtered off to afford 6.2 gr of the (−)-isomer of the sulfimide, $[\alpha]_D^{25} = -94.3°$ (optical purity, 96.2%). Similarly, these processes were repeated several times and

afforded either (+)- or (−)-enantiomer of the sulfimide with more than 95% optical purity.

(−)-trans-2,3-*Dibenzoylaziridine*. Into 3 ml of benzene containing *trans*-1,2-dibenzoylethylene (295 mg) (+)-(*R*)-*o*-methoxyphenylphenyl free sulfimide (364 mg, optical purity, 84.8%) was added at room temp, and the soln was kept standing at room temp for 1 hr. Then after benzene was removed *in vacuo*, the residue was chromatographed through a column packed with silica gel using $CHCl_3$ as an eluent, and then *trans*-2,3-dibenzoylaziridine ($[\alpha]_D^{25} = -32.9°$ ($CHCl_3$, $c = 1.9$)) was obtained in 30% yield together with 1-amino-1,2-dibenzoylethylene (68%), *o*-methoxyphenyl phenyl sulfide (100%). Recrystallization of the crude aziridine from MeOH gave racemic crystals while the aziridine recovered from the filtrate has a higher optical rotation. All the products obtained were identified from their IR and NMR spectra.

Reaction of dibenzoylethylene with (+)-(R)-o-methoxyphenylphenyl free sulfimide in methanol. trans-1,2-Dibenzoylethylene (300 mg) and (+)-(*R*)-*o*-methoxyphenylphenyl free sulfimide (322 mg, optical purity, 96.8%) were dissolved in 15 ml of MeOH at 30° and the soln was kept at 30° for 1 hr. When the soln was concentrated to 5 ml *in vacuo*, the crystals which were identified as the enaminoketone were collected and then the solvent was evaporated *in vacuo*. The residue was chromatographed similarly, affording (−)-*trans*-2,3-dibenzoylaziridine.

Reaction of dibenzoylethylene in dimethyl sulfoxide (DMSO). trans-1,2-Dibenzoylethylene (200 mg) and (+)-(*R*)-*o*-methoxyphenylphenyl free sulfimide (215 mg) were dissolved in 5 ml of DMSO at 28° and the soln was kept at 28° for 1 hr. Then, the soln was poured onto ice water. The aqueous soln was extracted with $CHCl_3$. The $CHCl_3$ layer was washed with water, dried over Na_2SO_4. After the usual work up, the products as shown in the Table 3 were obtained.

Reaction of cis-1,2-Dibenzoylethylene in benzene. cis-1,2-Dibenzoylethylene (400 mg) and (+)-(*R*)-*o*-methoxyphenylphenyl free sulfimide (196 mg, optical purity, 96.8%) were dissolved in 3 ml of benzene at room temp. After 1 hr, the soln was treated similarly. Thus, the corresponding sulfide (50%), *trans*-1,2-dibenzoylethylene (31%), *cis*-1,2-dibenzoylethylene (19%), *trans*-1-amino-1,2-dibenzoylethylene (21%) and (−)-*trans*-2,3-dibenzoylaziridine (33%) were obtained, $[\alpha]_D^{25} = -35.6°$ ($CHCl_3$, $c = 2.4$).

(+)-trans-2,3-*Dibenzoylaziridine*. *trans*-1,2-Dibenzoylethylene (200 mg) was treated with 1.2 molar equivalent of (−)-(*S*)-*o*-methoxyphenylphenyl free sulfimide ($[\alpha]_D^{25} = -191.6°$ ($CHCl_3$, $c = 2.0$), optical purity, 98.5%) in 3 ml of benzene at 20° for 1 hr. After the work up process, (+)-*trans*-2,3-dibenzoylaziridine was obtained in 59.4% yield, $[\alpha]_D^{25} = +23.2°$ ($CHCl_3$, $c = 2.0$). The structure was identified by IR and NMR.

(−)-trans-2-*Benzoyl*-3-*phenylaziridine*. Benzalacetophenone (200 mg) and (+)-(*R*)-*o*-methoxyphenylphenyl free sulfimide (266 mg, optical purity, 96.8%) were dissolved in 4 ml of benzene, and the mixture was heated at 50° for 48 hr. After the usual work up, the corresponding sulfide (100%) and (−)-*trans*- **7** (96%) were obtained, $[\alpha]_D^{25} = -99.9°$ ($CHCl_3$, $c = 3.4$). The optical rotation of **7** increased by several repeated recrystallizations from MeOH, attaining finally $[\alpha]_D^{25} = -306.8°$ ($CHCl_3$, $c = 0.4$), mp. 123.5–124.5°.

Solvent effect in the asymmetric induction of benzalacetophenone. Benzalacetophenone (100 mg) and (+)-(*R*)-*o*-methoxyphenylphenyl free sulfimide (126 mg) were dissolved in 10 ml CH_2Cl_2 or MeOH. The reaction was carried out at 50° or room temp. By the same work up process, the optically active aziridine was separated. The yield and optical rotation of the aziridine are shown in the Table 3.

(−)-trans-2-*Acetyl*-3-*phenylaziridine*. Benzalacetone (150 mg) and (+)-(*R*)-*o*-methoxyphenylphenyl free sulfimide (307 mg) were dissolved in 5 ml of benzene and the mixture was heated at 50° for 24 hr. After the same work up, (−)-*trans*-2-acetyl-3-phenylaziridine was obtained as an oil in 23% yield, $[\alpha]_D^{25} = -60.0°$ ($CHCl_3$, $c = 0.4$). IR (film, cm^{-1}), 3250, 1700. NMR (δppm), 2.35 (s, 3H, CH_3), 2.75 (s, 1H, NH), 2.92 (d, 1H, —CH—), 3.10 (d, 1H, —CH—, J = 2 Hz), 7.28 (m, 5H, Ph).

(+)-trans-2-*Benzoyl*-3-*phenylaziridine*. Benzalacetophenone (200 mg) was treated with 1.2 molar equivalent of (−)-(*S*)-*o*-methoxyphenylphenyl free sulfimide ($[\alpha]_D^{25} = -168.5°$, optical purity, 86.9%) in 3 ml CH_2Cl_2 at 50° for 48 hr. After the usual work up, (+)-*trans*-2-benzoyl-3-phenylaziridine was obtained in 21.8% yield, $[\alpha]_D^{25} = +77.5°$ ($CHCl_3$, $c = 0.85$, optical purity, 25.3%). The optical rotation of this compound increased to +101.9° by one recrystallization from MeOH.

(−)-2,2-*Dicarbomethoxy*-3-*phenylaziridine*. Benzylidene malonate (200 mg) was treated with 1.2 molar equivalent of (+)-(*R*)-*o*-methoxyphenylphenyl free sulfimide ($[\alpha]_D^{25} = +152.8°$, optical purity, 78.8%) in CH_2Cl_2 at 50° for 48 hr. After the usual work up, (−)-2,2-dicarbomethoxy-3-phenylaziridine was obtained as yellow oil in 41.9% yield together with *o*-methoxyphenyl phenyl sulfide (92.6%), $[\alpha]_D^{25} = -22.0°$ ($CHCl_3$, $c = 1.7$). IR (film, cm^{-1}), 3340, 1740. NMR (δppm), 3.18 (s, broad, 1H), 3.83 (s, broad, 6H), 4.42 (s, broad, 1H), 7.20–8.20 (m, 5H).

CD-measurement. CD spectra of the aziridines and cyclopropane were measured at 25° in EtOH soln of which the concentration was 8.25×10^{-5} mol/l for (−)-**7**, 1.08×10^{-4} mol/l for (+)-**7**, and 9.19×10^{-5} mol/l for **12**.

Determination of absolute configuration of 1,2-*dibenzoyl*-3-*phenylaziridine*

(−)-*trans*-1,2-*Dibenzoyl*-3-*phenylaziridine*. Optically pure (−)-trans-2-benzoyl-3-phenylaziridine (500 mg) was dissolved in 3 ml of dry pyridine. To this soln was added benzoyl chloride (470 mg) dropwise with stirring at 0°. After 30 min, the mixture was poured onto ice cold water. The ppt was filtered off and the corresponding N-benzoylaziridine was obtained quantitatively. The crude crystals were recrystallized from benzene-hexane, mp. 129–129.5°, $[\alpha]_D^{25} = -207.1°$ ($CHCl_3$, $c = 1.9$).

Iodide ion catalyzed rearrangement of (−)-trans-1,2-*Dibenzoyl*-3-*phenylaziridine*. The compound (550 mg) and NaI (800 mg) was dissolved in 10 ml of acetone and the mixture was refluxed for 3 hr. The process and the work-up procedure were carried out following the Padwa's method[14] mp. 103° (racemic form), $[\alpha]_D^{25} = -45.4°$ ($CHCl_3$, $c = 1.6$). NMR (δppm), 5.45 (AB, 2H, —CH—CH—), 7.2–8.1 (m, 15H, Ph).

Bayer-Villiger rearrangement of (−)-trans-2,4-*diphenyl*-5-*benzoyl*-2-*oxazoline*. The oxazoline (200 mg) and *m*-chloroperbenzoic acid (160 mg) were dissolved in 2 ml CH_2Cl_2 and the mixture was stirred overnight at room temp. The ppts were filtered off and the filtrate was removed *in vacuo*. The residue was chromatographed through a column packed with silica gel using $CHCl_3$ as an eluent. 2,4-Diphenyl-5-benzoyloxy-2-oxazoline (167 mg, 80%) was obtained, mp. 120–1° (recrystallized from MeOH), $[\alpha]_D^{25} = -185.9°$ ($CHCl_3$, $c = 1.2$). Found; C, 76.79, H, 4.74, N, 4.15. $C_{22}H_{17}NO_2$, Calcd; C, 76.95, H, 4.99, N, 4.07%). IR (KBr, cm^{-1}), 1725, 1655, 1265, 1055, 975. NMR (δ ppm), 5.13 (d, 1H, =N—CH—, J = 3 Hz), 6.48 (d, 1H, —CH<O—/O—>, J = 3 Hz), 7.0–8.0 (m, 15H, Ph).

Hydrolysis and reduction of (−)-2,4-*diphenyl*-5-*benzoyloxy*-2-*oxazoline*. The oxazoline (71 mg) and $NaBH_4$ (39 mg) were dissolved in 2 ml of EtOH. To this mixture was added 0.1 ml of 2% ethanolic KOH with stirring. After 10 min, 50 ml of water was added. The ppt

was filtered off and 2-benzoylamino-2-phenylethanol (30 mg, 60%) was obtained, mp. 179–180°, $[\alpha]_D^{25} = -18.0°$ (EtOH, $c = 0.4$).

(+)-(R)-2-*Benzoylamino-2-phenylethanol.* (−)-(R)-Phenylglycine (500 mg) was dissolved in 5 ml THF. To this soln was added LAH (380 mg) at room temp. The soln was kept until the hydride was consumed. After quenching the mixture with water, the aqueous soln was extracted with CH_2Cl_2. The 2-phenylethanolamine was obtained by chromatography through a column packed with silica gel as an oil in 8.8% yield (40 mg), $[\alpha]_D^{25} = -45.5°$ ($CHCl_3$, $c = 0.5$). 2-Phenylethanolamine (40 mg) was treated with benzoyl chloride (123 mg) in pyridine soln at room temp, then the mixture was added into an aqueous methanolic soln containing KOH, and the N-benzoyl derivative was obtained as a ppt. The ppt was then filtered off, dried to give 14.7 mg of the product, $[\alpha]_D^{25} = +19.7°$ (EtOH, $c = 0.15$).[24]

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